REMARKS

Claims 22-27 are pending in this application. Claims 1-21 have been canceled without prejudice or disclaimer. Claims 22-26 have been amended. Claim 27 has been newly added.

Claims 1-21 have been canceled without prejudice or disclaimer, and claims 22-26 have been amended, for the sole reason of advancing prosecution. Applicants, by canceling or amending any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert any of the claims canceled herein or the original claim scope of any claim amended herein, in a continuing application.

Claim 22 has been amended to recite a "method for treating atrophy or aging of skin in women, comprising: administering to a female subject in need thereof, a topical skin preparation comprising a testosterone ester of an acid having between six to eleven carbon atoms, provided that the topical skin preparation does not comprise estrogen or estrogen derivatives." Support for claim 22, as amended, can be found throughout the specification and claims as originally filed. No new matter has been added.

Claims 23-26 have each been amended to correct dependency and antecedent basis. Support for claims 22-26, as amended, can be found throughout the specification and claims as originally filed. No new matter has been added.

Claim 27 has been newly added. New claim 27 is directed to the "method according to claim 22, wherein the testosterone phenyl propionate is present in a concentration of

from 0.1 to 1% by weight of the total preparation"

In view of the remarks set forth below, further and favorable consideration is respectfully requested.

I. At page 2 of the Official Action, the Examiner acknowledges the claim of priority to the effective filing date of International Application PCT/IL2004/00074.

The Examiner indicated that the disclosure of Israeli Patent Application No. 157535, filed August 21, 2003, does not provide adequate support for claim 24 of the present application. Accordingly, the Examiner acknowledges the claim of priority to PCT/IL2004/00074. However, while making no assertion regarding the claim of priority with relation to claim 24, Applicants respectfully remind the Examiner that priority is determined on a claim by claim basis. Accordingly, Applicants respectfully request that the Examiner also ***acknowledge Applicants' claim of priority to Israeli Patent Application No. 157535 for at least claims 22-23 and 25-27***. With specific regard to new claim 27, Applicants submit that support for claim 27 can be found at page 3 of Israeli Patent Application No. 157535.

II. At page 2 of the Official Action, claim 22 has been objected to.

The Examiner objects to claims 22 as reciting the incorrect spelling of the term "derivatives." Applicants respectfully submit that, as amended, claim 22 no longer recites the improper spelling of "derivatives." Accordingly, the Examiner is respectfully requested to withdraw this objection.

III. At page 3 of the Official Action, claims 23-26 have been rejected under 35 USC § 112.

The Examiner asserts that claims 23-26 are not compliant with 35 USC § 112, as are improperly dependent.

Applicants respectfully submit that each of claims 23-26 have been amended to correct claim dependency. Accordingly, each of the pending claims 23-26 no longer depend from cancelled claims.

In view of the amendments to claims 23-26, Applicants respectfully submit that the rejections under 35 USC § 112 have been obviated. In this regard, Applicants submit that all of the presently pending claims fully comply with 35 USC § 112. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

IV. At page 4 of the Official Action, claim 22 has been rejected under 35 USC § 102(e) as being anticipated by Mazer et al. (US Patent No. 6,583,129).

The Examiner asserts that Mazer et al. teach each and every element of claim 22.

In view of the remarks set forth herein, this rejection is respectfully traversed.

The test for anticipation is whether each and every element as set forth is found, either expressly or inherently described, in a single prior art reference. Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP § 2131. The identical invention must be shown in as complete detail as is contained in the claim. Richardson v. Suzuki Motor Co., 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); MPEP §2131. The elements must also be arranged as required by the claim. In re Bond, 15 USPQ2d 1566 (Fed. Cir. 1990).

Amended claim 22 is directed to a method for treating atrophy or aging of skin in women, comprising: administering to a female subject in need thereof, a topical skin preparation comprising a testosterone ester of an acid having between six to eleven carbon atoms, provided that the topical skin preparation does not comprise estrogen or estrogen derivatives.

In contrast to the presently pending subject matter, Mazer et al. is directed to compositions, methods, and kits to treat women with elevated SHBG levels, or women receiving oral estrogen supplementation, by administering an amount of an androgenic steroid. *See* Mazer et al., at the abstract.

From the outset, Applicants note that while claim 1 of Mazer et al. recites "a method of improving health" it does not teach a method for the treatment of atrophy or aging of the skin as recited in present claim 22. As defined in column 8, lines 39-51, of Mazer et al., the phrase "improving health" refers to various health conditions which are not specifically related to atrophy or aging of the skin. In this regard, according to Mazer et al.:

> 'Improving health' refers to reducing, improving, or preventing the incidence and/or intensity of symptoms associated with androgenic steroid deficiency. Examples of such symptoms include but are not limited to: sexual dysfunction, which can manifest in loss of sexual desire, decreased sensitivity to sexual stimulation, decreased arousability and capacity for orgasm, diminished vital energy, depressed mood, diminished sense of well-being, increased shyness, loss of muscle mass and function, unfavorable body composition, i.e., lean to fat mass ratio, thinning and loss of pubic hair, urogenital atrophy, dry and brittle scalp hair, dry skin, decreased cognitive abilities, dry eyes, autoimmune phenomena, and a combination thereof. *See* Mazer et al. at column 8, lines 39-51.

Applicants respectfully submit that nowhere in Mazer et al. is a method for the treatment of atrophy or aging of the skin taught or suggested.

Additionally, Applicants submit that Mazer et al. do not teach administration of a topical skin preparation that ***does not comprise estrogen or estrogen derivatives***, as recited in claim 22. In contrast, in each of "the Examples" in Mazer et al., a method for the treatment of atrophy or aging of the skin comprising the administration of a topical preparation that does not comprise estrogen is not taught. *See* Mazer et al., for example at Example 2-4.

Accordingly, Applicants submit that Mazer et al. do not teach each and every element of amended claim 22, as required for anticipation under 35 USC § 102(b). Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claim 22 under 35 USC § 102(b).

V. At page 5 of the Official Action, claims 22 and 23 have been rejected under 35 USC § 103(a) as being obvious over Mazer et al. in view of Shouls et al. (Shouls et al., Contact Allergy to Testosterone in an Androgengenic Patch: Control of Symptoms by Pre-application of Topical Corticosteroid, 45 Cont. Dermatitis 124 (2001)).

The Examiner asserts that it would have been obvious to one of ordinary skill in the art to combine the teachings of Shouls et al. with that of Mazer et al. to arrive at the presently claimed subject matter because both the testosterone derivatives of Mazer et al. and the testosterone phenyl propionate of Shouls et al. have been indicated as suitable for transdermal therapy.

In view of the following, this rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court very recently held in *KSR International Co. v. Teleflex Inc. et al.*, Slip Opinion No. 04–1350, 550 U. S. ____ (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR*, *supra*, slip opinion at 13-15.) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

With regard to motivation to combine references, **MPEP 2143** discusses the requirements of a *prima facie* case of obviousness. First, there must be some suggestion or motivation to combine the reference teachings or to modify the reference, and second, there must be a reasonable expectation of success. Finally, the prior art reference or references when properly combined, must teach or suggest all the claim limitations.

Regarding motivation to modify properly combined references, **MPEP 2143.01** states that a proposed modification cannot render the prior art unsatisfactory for its intended purpose. If it does, then there is no suggestion or motivation to make the proposed modification. Further, the proposed modification cannot change the principle operation of a reference.

Regarding *teaching away*, **MPEP 2141.02** states that prior art must be considered in its entirety, including disclosures that *teach away* from the claims. See also **MPEP 2145(X)(D)**. The Federal Circuit in *Takeda v. Alphapharm* found that the prior art taught away from the closest compound because the prior art in fact disclosed a broad selection of compounds where the closest prior art compound exhibited negative properties that would have led the skilled artisan away from that compound.

Applicants respectfully submit that a *prima facie* case of obviousness has not been established because, whether taken alone or in combination, none of the cited references teach or suggest each and every element of the presently pending claims and there is no motivation to modify the topical formulation of Mazer et al. with the ***injectable testosterone propionate*** described in Shouls et al.

As discussed above, claim 22 is directed to a method for treating atrophy or aging of skin in women, comprising: administering to a female subject in need thereof, a topical skin preparation comprising a testosterone ester of an acid having between six to eleven carbon atoms, provided that the topical skin preparation does not comprise estrogen or estrogen derivatives. Claims 23 depends from claim 22.

In contrast to the presently pending subject matter, Mazer et al. is directed to compositions, methods, and kits to treat women with elevated SHBG levels, or women receiving oral estrogen supplementation, by administering an amount of an androgenic steroid. *See* Mazer et al., at the abstract. Unlike the presently claimed subject matter, Mazer et al. do not teach or suggest a method for the treatment of atrophy or aging of the skin, as recited in present claim 22. In addition, Applicants submit that Mazer et al. do not teach or suggest the administration of a topical skin preparation that ***does not comprise estrogen or estrogen derivatives***, as recited in claim 22.

Shouls et al. do not remedy the deficiencies of Mazer et al. Shouls et al. describe contact allergies associated Andropatch®, i.e. a testosterone containing transdermal patch. However, like Mazer et al., Shouls et al. do not teach or suggest a method for the treatment of atrophy or aging of the skin, as recited in present claim 22. In addition, Applicants submit that neither Mazer et al. nor Shouls et al. teach or suggest the administration of a topical skin preparation which ***does not comprise estrogen or estrogen derivatives***, as recited in claim 22.

With regard to testosterone phenylproprionate, nowhere in Shouls et al. is testosterone phenylproprionate taught or suggested in a transdermal dosage form. In this regard, Applicants submit that Andropatch® contains testosterone and not testosterone phenylproprionate. The only reference to testosterone phenylproprionate in Shouls et al. is with regard to injectable compositions, for example, Sustanon 100 and Viromone. Please *see* Shouls et al. at page 44, Table 1. Accordingly, Applicants submit that Shouls et al. provides no teaching or suggestion of testosterone phenylproprionate in a transdermal patch. Therefore, whether taken alone or in combination neither Mazer et al. nor Shouls et al. teach or suggest every element of the presently claimed subject matter.

Furthermore, Applicants submit that there would be no motivation to modify the transdermal composition described in Mazer et al. with the injectable dosage forms described in Shouls et al. Applicants submit that there is no evidence that testosterone derivatives such as, testosterone phenylproprionate, would have any action in a topical dosage form. The Examiner is politely reminded that a proposed modification cannot render the cited art unsatisfactory for its intended purpose. If it does, then there is no suggestion or motivation to make the proposed modification. Further, the proposed modification ***cannot*** change the principle operation of a reference. *See* **MPEP § 2143.01**. Accordingly, Applicants submit that the presently claimed subject matter is not obvious in view of the cited art.

In view of the remarks set forth herein, it is submitted that, whether taken alone or in combination, Mazer et al. and Shouls et al. do not render claims 22-23 obvious within the meaning of 35 USC § 103 (a). Accordingly, the Examiner is respectfully requested to withdraw this rejection.

VI. At page 5 of the Official Action, claims 22-26 have been rejected under 35 USC § 103(a) as being obvious over Mazer et al. in view of De Nijis et al. (US Patent Application No. 2005/0101517) and Friedman (US Patent No. 6,004,566).

The Examiner asserts that it would have been obvious to one of ordinary skill in the art to combine Mazer et al. with De Nijis et al. and Friedman et al. to arrive at the presently claimed subject matter because it would have been obvious to utilize the testosterone phenylpropionate described in De Nijis et al. in amounts taught in Friedman et al. in the composition described by Mazer et al. and because the testosterone phenylpropionate of Shouls et al. has been indicated as suitable for transdermal therapy.

In view of the following, this rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court very recently held in *KSR International Co. v. Teleflex Inc. et al.*, Slip Opinion No. 04–1350, 550 U. S. ____ (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an

apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR*, *supra*, slip opinion at 13-15.) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

With regard to motivation to combine references, **MPEP 2143** discusses the requirements of a *prima facie* case of obviousness. First, there must be some suggestion or motivation to combine the reference teachings or to modify the reference, and second, there must be a reasonable expectation of success. Finally, the prior art reference or references when properly combined, must teach or suggest all the claim limitations.

Regarding motivation to modify properly combined references, **MPEP 2143.01** states that a proposed modification cannot render the prior art unsatisfactory for its intended purpose. If it does, then there is no suggestion or motivation to make the proposed modification. Further, the proposed modification cannot change the principle operation of a reference.

Regarding *teaching away*, **MPEP 2141.02** states that prior art must be considered in its entirety, including disclosures that *teach away* from the claims. See also **MPEP 2145(X)(D)**. The Federal Circuit in *Takeda v. Alphapharm* found that the prior art taught away from the closest compound because the prior art in fact disclosed a broad selection of compounds where the closest prior art compound exhibited negative properties that would have led the skilled artisan away from that compound.

Applicants respectfully submit that a *prima facie* case of obviousness has not been established because, whether taken alone or in combination, none of the cited references teach or suggest each and every element of the presently pending claims and there is no motivation to modify the topical formulation of Mazer et al. with the ***injectable testosterone propionate*** described in Friedman et al.

As discussed above, claim 22 is directed to a method for treating atrophy or aging of skin in women, comprising: administering to a female subject in need thereof, a topical skin preparation comprising a testosterone ester of an acid having between six to eleven carbon atoms, provided that the topical skin preparation does not comprise estrogen or estrogen derivatives. Claims 23-27 depend, either directly or indirectly, from claim 22.

In contrast to the presently pending subject matter, Mazer et al. is directed to compositions, methods, and kits to treat women with elevated SHBG levels, or women receiving oral estrogen supplementation, by administering an amount of an androgenic steroid. *See* Mazer et al., at the abstract. Unlike the presently claimed subject matter, Mazer et al. do not teach or suggest a method for the treatment of atrophy or aging of the

skin, as recited in present claim 22. In addition, Applicants submit that Mazer et al. do not teach or suggest the administration of a topical skin preparation that does not comprise estrogen or estrogen derivatives, as recited in claim 22.

De Nijis et al. do not remedy the deficiencies of Mazer et al. De Nijis et al. is directed to formulations of testosterone decanoate for use in humans. However, like Mazer et al., De Nijis et al. do not teach or suggest a method for the treatment of atrophy or aging of the skin, as recited in present claim 22. In addition, Applicants submit that neither Mazer et al. nor De Nijis et al. teach or suggest the administration of a topical skin preparation which does not comprise estrogen or estrogen derivatives, as recited in claim 22.

Freidman et al. do not remedy the deficiencies of Mazer et al. and De Nijis et al. Friedman et al. is directed to a delivery system that includes a bioactive drug or cosmetic substance presented in the form of submicron oil spheres alone, or drugs or cosmetic substances in a combination with the oil spheres in an aqueous suspension or emulsion. *See* Friedman et al. at the abstract. However, like Mazer et al. and De Nijis et al., Freidman et al. do not teach or suggest a method for the treatment of atrophy or aging of the skin, as recited in present claim 22. In addition, Applicants submit that none of Mazer et al., De Nijis et al. and Freidman et al. teach or suggest the administration of a topical skin preparation which ***does not comprise estrogen or estrogen derivatives***, as recited in claim 22.

With regard to testosterone phenylproprionate, nowhere in De Nijis et al. is testosterone phenylproprionate taught or suggested in a transdermal dosage form. In this regard, Applicants submit that that Sustanon® is an injectable dosage form of a combination of various esterized testosterone compounds. ***Sustanon® is not indicated for transdermal use***. Please *see* http://www.sustanon.com/.

As such, Applicants submit that there would be no motivation to modify the transdermal composition described in Mazer et al. with the injectable testosterone ester combination described in De Nijis et al. Applicants submit that there is no evidence that testosterone derivatives such as, testosterone phenylproprionate, would have any action in a topical dosage form. The Examiner is politely reminded that a proposed modification cannot render the cited art unsatisfactory for its intended purpose. If it does, then there is no suggestion or motivation to make the proposed modification. Further, the proposed modification cannot change the principle operation of a reference. *See* **MPEP § 2143.01**. Accordingly, Applicants submit that the presently claimed subject matter is not obvious in view of the cited art.

In view of the remarks set forth herein, it is submitted that, whether taken alone or in combination, Mazer et al., De Nijis et al. and Friedman et al. do not render claims 22-27 obvious within the meaning of 35 USC § 103 (a). Accordingly, the Examiner is respectfully requested to withdraw this rejection.

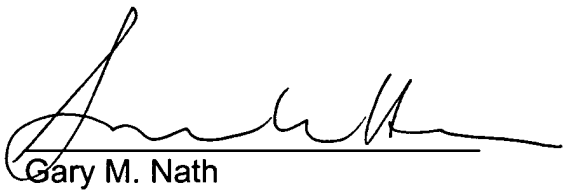
CONCLUSION

In view of the foregoing, Applicants submit that the application is in condition for immediate allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

THE NATH LAW GROUP



Gary M. Nath
Registration No. 26,965
Susanne M. Hopkins
Registration No. 33,247
Ari G. Zytcer
Registration No. 57,474
Customer No. 20259

Date: December 19, 2008
THE NATH LAW GROUP
112 South West Street
Alexandria, VA 22314
Tel: (703) 548-NATH
Fax: (703) 683-8396